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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/992,235	11/06/2001	Seth Lederman		5392

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EXAMINER	
ROYDS, LESLIE A	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/992,235	LEDERMAN ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8 are presented for examination.

Applicant is notified that the finality of the previous Office Action dated December 28, 2007 is hereby withdrawn. The after-final amendment filed May 6, 2008 has been entered into the record and prosecution of the present application has been reopened.

Applicant's after-final amendment filed May 6, 2008 has been received and entered into the instant application.

Claims 1-8 remain pending and under examination. Claims 23-24 are cancelled.

Applicant's arguments and amendments, filed May 6, 2008, have been fully considered. Regrettably, however, the allowability of the instant claims is hereby withdrawn upon reconsideration of the present claim set and the prior art. Accordingly, the following rejections and objections are newly applied and constitute the complete set of rejections and objections applied to the instant claims.

Warning Regarding Substantially Duplicate Claims

Applicant is advised that should claim 7 be found allowable, claim 8 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Salvesen et al. ("NMR and ORD Determination of the Configuration of N-Cyanobenzylamphetamine (AN 1)", *Aezneim-Forsch. (Drug Res.)*, 1974; 24(2):137-140; already of record), in light of STN Registry File No. 17590-01-1 ("Amphetaminil", 2008) and Stedman's Medical Dictionary (Twenty-Second Edition, 1972; p.377), each cited to show facts, in view of Remington's Pharmaceutical Sciences (Sixteenth Edition, 1980; p.420-425).

Salvesen et al. teaches that the compound N-cyanobenzylamphetamine (also known as AN1; col.1, para.1, p.137) is marketed in dragees with a content of 10 mg α-phenyl-α'-N-(beta-phenylisopropylamino) acetonitrile, which has a general stimulant effect (col.1, para.1, p.137). Salvesen et al. further teaches that the compound can exist in two diastereoisomeric forms (col.1, para.2, p.137) and discloses that synthesis of N-cyanobenzylamphetamine from S-(+)-amphetamine renders a diastereoisomeric mixture of [(αS,α'R), (αS, α'S)] N-cyanobenzylamphetamine and the synthesis of the same from R-(-)-amphetamine renders the diastereoisomeric mixture of [(αR,α'R), (αR,α'S)] N-cyanobenzylamphetamine (col.2, para.4, p.138), thus, supporting the conclusion that four stereoisomers of the compound N-cyanobenzylamphetamine were known and identified in the art (col.2, para.6, p.138).

STN Registry File No. 17590-01-1 is cited for its teaching that the term N-

cyanobenzylamphetamine, or "AN1", and the term "α-phenyl-α'-N-(beta-phenylisopropylamino) acetonitrile" are each synonymous with amphetaminil as used in instant claim 1. This is further supported by the fact that the chemical structure disclosed by Salvesen et al. as being N-cyanobenzylamphetamine is identical to the chemical structure disclosed by STN Registry File No. 17590-01-1 as amphetaminil.

Stedman's Medical Dictionary (Twenty-Second Edition, 1972; p.377) is cited to show that dragees are sugar-coated pills or capsules. Accordingly, the very fact that Salvesen et al. teaches a formulation of the disclosed N-cyanobenzylamphetamine compound necessarily requires, though not explicitly stated in Salvesen et al., sugar to coat the pill or capsule to form the dragees. As a result, the inherent presence of sugar in the dragee formulation necessarily meets Applicant's limitation directed to "at least one pharmaceutically acceptable carrier, diluent, excipient or additive" as recited in instant claim 1.

Salvesen et al. fails to teach a pharmaceutical composition comprising a pharmaceutically acceptable salt of (R,R'),(R,S')-amphetaminil substantially free of a pharmaceutically acceptable salt of (S,R'), (S,S')-amphetaminil (claim 1) or a controlled or immediate release formulation thereof (claims 2-3).

Though it is noted that Salvesen et al. teaches a formulation containing a racemic mixture of the four stereoisomeric configurations of N-cyanobenzylamphetamine (i.e., amphetaminil) and fails to expressly teach a pharmaceutically acceptable salt of (R,R'),(R,S')-amphetaminil substantially free of a pharmaceutically acceptable salt of (S,R'), (S,S')-amphetaminil, one of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to modify the stereoisomeric mixture of the compound N-cyanobenzylamphetamine (i.e., amphetaminil) (col.2, para.6, p.138), as disclosed by Salvesen et al., to contain the isomeric configurations with the greatest activity over the others because isomers of a racemic mixture are reasonably expected to have differing activities such that particular isomers are generally expected to be more active than others due to the fact that living systems are chiral

and, thus, preferentially process certain stereochemical configurations over others. In other words, optically active isomer isolation from a racemic mixture would have been *prima facie* obvious to one of skill in the art at the time of the invention due to the reasonable expectation of greater activity from one isomer over the other. Motivation to isolate isomeric configurations from a disclosed mixture flows logically from the desirability of producing a pharmaceutical composition that will produce an optimal therapeutic effect. Please reference *In re Anthony*, 162 USPQ 594, and *In re Adamson*, 125 USPQ 233. Moreover, in consideration of the fact that the skilled artisan would have been reasonably apprised of conventional methods of isolation and purification, such as various chromatographic methods, the artisan would have predictably used such methods within the knowledge and possession of one of ordinary skill in the art to isolate and concentrate the desired isomeric configurations to meet the instantly claimed percentage concentrations (see, e.g., instant claims 6-8, which specify that the composition contains greater than 90% or greater than 95% of the desired isomeric configurations) with the greatest pharmacologic activity for use in the pharmaceutical formulation.

Remington's Pharmaceutical Sciences (p.420-425) teaches that drugs are formulated into salts to modify the duration of action of a drug; to modify the transportation and distribution of the drug in the body; to reduce toxicity; and to overcome difficulties encountered in pharmaceutical formulation procedures or in the dosage form itself (col.2, p.424, para.1).

One of ordinary skill in the art at the time of the present invention would have found it *prima facie* obvious to employ a salt formulation of the desired pharmacologically active isomers with the greatest activity of the N-cyanobenzylamphetamine compound (i.e., amphetaminil) as disclosed by Salvesen et al. because, as evidenced by Remington's, pharmaceutical salt formulations are known to modify the duration of action of a drug, modify the transportation and distribution of the drug in the body, reduce toxicity, and to overcome difficulties encountered in pharmaceutical formulation procedures or in the dosage form itself. Thus, it would have been *prima facie* obvious to the skilled artisan motivated by

any one or more of these factors to formulate the desired pharmacologically active isomers with the greatest activity of the N-cyanobenzylamphetamine compound (i.e., amphetaminil) of Salvesen et al. into a pharmaceutically acceptable salt to enhance the pharmacokinetic parameters of the drug or to reduce the toxicity with the reasonable expectation that the therapeutic benefit of the agent in salt form would have been the same or substantially similar to that of the parent amphetaminil compound itself.

Regarding the claimed limitation directed to a controlled release formulation of the claimed composition (claim 2) or an immediate release formulation of the claimed composition (claim 3), such limitations of the instant claims fails to patentably distinguish the instant claims over the copending claims because the limitation of present claim 2 describing the composition as a "controlled release formulation" or the limitation of present claim 3 describing the composition as an "immediate release formulation" are each intended uses of the composition (i.e., an intent to use the disclosed composition as a controlled or immediate release formulation), which do not impart any physical or material characteristics to the composition that are not already present in the copending claims. If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble of not considered a limitation and is of no significance to claim construction. See *Pitney Bowes, Inc. v. Hewlett-Packard Co.,* 182 F.2d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999). See also *Rowe v. Dror*, 112 F.3d 473, 378, 42 USPQ2d 1550, 1554 and MPEP §2112.02(II). In the instant case, the cited prior art meets each and every structural and physical limitation of the instantly claimed "controlled release" or "immediate release" composition and, thus, would be reasonably expected to be capable of performing the intended use as instantly claimed, absent factual evidence to the contrary and further absent any apparent structural difference between the composition of the prior art and that of the instant claims.

Conclusion

Rejection of claims 1-8 is proper.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

June 6, 2008

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614